

July 21, 2004

Food and Drug Administration  
Docket No. 2003N-0342  
RIN 0910-AC35  
Division of Dockets Management  
5630 Fishers Lane  
Room 1061  
Rockville, MD 20852

**Subject: Toll-Free Number for Reporting Adverse Events on Labeling for Human Drug Products**

To Whom It May Concern:

The National Association of Chain Drug Stores (NACDS) is providing comments on the agency's implementation of Section 17 of the Best Pharmaceuticals for Children Act of 2001 (P.L. 107-109) that requires pharmacies to include as part of the labeling of each consumer prescription package a toll-free number maintained by the Secretary of HHS to report to the FDA adverse reactions from medications. This statement or phrase proposed by the FDA is "Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088." See 69 Fed. Reg. 21 778 (April 22, 2004).

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NACDS represents more than 200 chain pharmacy companies that operate nearly 32,000 community retail pharmacies. NACDS membership is the largest provider of outpatient prescription medications, including information that helps patients understand how to take their medications appropriately. Our industry dispenses about 70 percent of all outpatient retail prescription drugs, and will be disproportionately impacted by this proposed regulation.

**FDA Should Provide Significant Additional Flexibility Consistent with Congressional Intent**

NACDS understands the need to enhance the reporting of post-marketing adverse drug reactions (ADRs) to the FDA. These reports help practitioners understand the impact of the broader use of medications beyond the limited population of patients included in clinical trials.

The law indicates that, "in promulgating the rule, the Secretary shall seek to minimize the cost of the rule on the pharmacy profession." The law also states that the toll free number is to be accompanied by a statement that "such a number is to be used for reporting purposes only, not to receive medical advice." We concur with the flexibility that the agency has proposed to give to pharmacists to provide this statement. However, the agency failed to take other steps that could have more effectively met the intent of the program, but would have further streamlined the program, making it more effective, and reducing the burden on pharmacists.

We are concerned that FDA's implementation of this program could result in little benefit to consumers, and may in fact compromise patient care. In addition, the agency has mandated that this statement be provided with all 3.1 billion prescriptions dispensed each year – new and refill – and for every drug that is currently on the market. Limiting the distribution of this statement, based on the pharmacist's discretion, to certain patients and for certain drugs would satisfy the intent of the program.

The agency could also have minimized the impact on pharmacy by requiring manufacturers of unit of use products, and those that have to distribute patient package inserts (PPIs) with their prescription packaging, to provide this number on their containers or on the PPI, obviating the need for pharmacies to generate this information.

In our view, implementation of this program in its proposed form will not only be burdensome to pharmacies, but will be extremely burdensome to FDA. That is because it will result in the reporting of thousands of insignificant, commonly-known adverse events of prescription drugs that have been on the market for decades. Instead, this program should be targeted to encourage consumer reporting of adverse reactions from newer drugs. Certain new side effects may be identified once a newer drug is used in the broader population, that were not identified in more limited clinical trials or early use experience.

However, by proposing a wide-ranging program in this proposed rule, rather than a more targeted and effective program, FDA runs the risk that the public will dismiss the importance of reporting adverse events. That could happen if the system becomes overwhelmed with reports of commonly-known adverse events (i.e. gastrointestinal distress with antibiotics; sleepiness with benzodiazepines). The agency may have no choice but to establish voice recording systems to allow all the patients calling in to the FDA to leave information about their suspected event. Because patients may not be able to reach the agency with more important unknown events for newer drugs, the relevance of this system will decline and important adverse events that are occurring from newer drugs could be missed.

We also believe that this proposed rule could create confusion among patients who will report adverse drug reactions (ADRs) to the FDA (or a recording system at FDA), rather than their physician or pharmacist. Despite the attempts to correctly direct patients to their health professionals, some may call the agency and leave information that is better sent to physicians or pharmacists for reporting.

Moreover, by not referring the patient to the "pharmacist" in the statement, the agency has overlooked a critical player in the identification and reporting of adverse events. We propose that the agency use the statement, "Call your health professional for advice about side effects. Report side effects to FDA at 1-800-FDA-1088," or "Call your doctor or pharmacist for advice about side effects. Report side effects to FDA at 1-800-FDA-1088." We also believe that it is important for the patient to understand that the FDA does not and will not offer medical advice about what to do about the side effect that might have been experienced.

### **Discussion of Options for Pharmacy Providers**

We agree that the agency should provide pharmacies with multiple options for satisfying the statement requirement. We oppose a requirement to place this statement directly on the label of the prescription vial or container, which in many cases is already too crowded.

State pharmacy practice laws and regulations already require that a significant amount of information be included on the prescription vial label, such as the name and address of the patient, prescription number, directions for use, expiration date, prescriber's name, pharmacy name, contact phone, and name or initials of pharmacist that filled the prescription, and even more information if the product is a controlled substance. Moreover, some states require that the physician's phone number be included on the label, so it is possible that two phone numbers already exist on the prescription label.

We agree that one option should allow the pharmacist to place the statement on an auxiliary label on the prescription package dispensed to the consumer. Prescription packaging also usually contains several auxiliary labels that highlight for the patient the most important facts to remember to take the medication appropriately. Pharmacists will have to weigh this particular option, however, with the goal of not excluding an important auxiliary label relating to the appropriate use of the drug, in order to accommodate the auxiliary label with the toll free number. The first goal of labeling should be to assure that the information on the prescription packaging helps the patient understand how to take the medication correctly and avoid ADRs in the first place. We are concerned that the addition of another auxiliary label could crowd out more important labels, and possibly reduce the importance that consumers ascribe to these labels if secondary information (unrelated to the appropriate use of the drug) is also on an auxiliary label, such as this statement.

Many pharmacy systems print auxiliary labels as part of a single pass document from the pharmacy computer system that includes, in addition to the prescription label, the necessary auxiliary labels, prescription receipt, consumer medicine information (known as CMI), third party prescription log information, and possibly coupons for the patient. Whether the statement is included as the auxiliary label or as part of the medication guide (an option that is described below), there are significant computer system program changes and tests that must be conducted before this statement can be generated from a complex, highly-integrated computer system. This includes possible changes to the "single pass" sheet design that may already be stocked in large quantities. Moreover, the database companies that produce this written consumer medicine information (CMI) would have to agree to modify the information that they license to pharmacies so the statement can be printed as part of the CMI. This may take some time to do, and we urge that the agency work with the database companies as soon as possible to discuss the feasibility of this option.

We also agree that other options to the pharmacist should include providing the number on a separate sheet of paper, on the voluntarily-provided CMI, or on a vial cap. We also believe that pharmacists should be permitted to place this statement on the bag in which the prescription is dispensed, if there is room on the bag and the pharmacy chooses to use this other option. This would obviate the need to provide another piece of paper, which may not be read by the patient. Finally, the pharmacist (or other entities that wanted to produce these for distribution) could provide a magnet to the patient to place on their refrigerator that would have the statement, including the FDA number. In this case, patients would not have to receive this information each and every time they pick up a prescription for themselves and/or family members.

We support the agency's interpretation that this statement should be included by pharmacists dispensing prescriptions from the multiple outpatient dispensing sites listed in the definition, including hospital outpatient pharmacy departments. In addition, physicians that dispense prescriptions should be required to provide this information as well. This will help assure that the rule meets congressional intent of assuring the widest possible dissemination of the number.

## **Reducing the Burden on Pharmacy Providers**

The agency could use its discretion and take the following steps to reduce the burden on pharmacies, as well as make the program more meaningful for patients:

**Limit Provision of Statement to New Drugs:** The agency should limit the requirement that pharmacies provide this statement to drugs that have been approved for marketing within five years of the date of the final rule, and for five years for new drugs approved after the rule is final. In fact, the agency should limit this program to the approximately 30 new molecular entities that are approved each year for the five-year period of time after they are approved. In our view, reports to FDA about ADRs that are commonly known and understood have little value. This program should be focused on generating new information about ADRs for newer drugs and newer molecular entities that are just beginning to become widely used in the population.

**Limit Provision of Statement to New Patients and Certain New Prescriptions:** The agency should allow pharmacies to only distribute this statement to existing patients of the pharmacy who are obtaining certain new prescriptions, and new patients of the pharmacy. Patients (and family members) that are long standing customers of a pharmacy will likely not need the information in the statement each and every time they obtain a prescription. Likewise, patients who are taking the same medication for a long time will likely be able to identify and manage their side-effects after taking the first course of prescription therapy, and will likely have discussed these issues with their health professional. Patients who are taking medications on a chronic basis will likely not find any value to receiving this required statement each and every time they obtain their prescription. Even for patients on existing drugs that are obtaining new prescriptions, the pharmacist should be able to use his or her judgment in distributing the statement if the pharmacist is reasonably sure that the patient already knows about the toll-free number.

**Requiring More Initiative of the Manufacturers:** While the agency indicates that it is exercising its discretion in giving affected pharmacies flexibility in complying with the law, it has failed to create a proportionate burden among the manufacturers. We agree with the agency's determination that this statement should be included in FDA-required and approved medication guides. Pharmacists would not have to distribute the statement with prescription drugs for which an FDA-mandated medication guide is required. However, there is no clear reason why manufacturers whose products include PPIs should not also include this statement in the information provided in their packages. This PPI information is developed for consumers, and will likely be read by them more than a separate piece of paper distributed by the pharmacist with this statement. In addition, these PPIs have been developed for drugs where side effects commonly occur, such as oral contraceptives and estrogens. Requiring manufacturers of these products to include these statements in PPIs would further reduce the burden to pharmacies and possibly enhance reporting.

FDA also failed to take steps to require manufacturers of unit of use products to place this statement on their packaging, which would significantly reduce the burden on pharmacies. About 15 percent of all currently-marketed drug products are in packages that are directly dispensed by pharmacies after applying the required prescription label. The industry is moving toward more unit of use packaging, given that this type of packaging can help enhance compliance and reduce potential repackaging and dispensing errors. Failing to require manufacturers to revise their exterior packaging labeling to include this statement is a major omission in the implementation of this regulation. It would significantly alleviate the cost and burden on pharmacies, as required under the law, and would appropriately spread the burden of this new law among all affected and interested parties.

Moreover, some patients ask pharmacists for the full FDA-approved prescribing information that accompanies prescription products. Patients may believe that this information is more accurate or comprehensive than any summary version of this information that they receive from pharmacies. While most pharmacies provide useful CMI, some patients simply like to have the full prescribing information as a reference. For that matter, the FDA should require that manufacturers of prescription products include this statement in all FDA-approved prescription labeling. This will assure that the number will receive the widest exposure, and will also help mitigate the impact on pharmacy.

**Electronic Options for Consumers and Pharmacies:** Many consumers now obtain prescription refills online, and some licensed pharmacies also allow patients to ask their pharmacist to call their physician to obtain a new prescription. Some pharmacies may e-mail a patient to indicate that the new prescription or refill prescription is ready. The pharmacy should be allowed to e-mail the FDA statement required under this proposed rule along with notice to the patients that their prescriptions are ready. Pharmacies should be able to send this information through an electronic means to patients who are familiar with computers. These patients are more likely to retain the statement, and possibly refer to it and use it later on, if it is sent electronically and stored in their computer. This should obviate the need for the pharmacy to provide the patient with a paper version of the statement when the prescription is picked up.

**Compliance Timeline:** NACDS recommends that pharmacies and affected dispensers be given no less than one year from the effective date of the final rule to comply with the statement requirement. This will give pharmacies appropriate time to test the different options proposed to provide this information to consumers. Also, use of the auxiliary label option is not as simple as the rule suggests. While the rule suggests that pharmacies may simply be able to buy these auxiliary labels with a statement, most pharmacies integrate the printing of these labels into their existing prescription processing systems.

In addition, we understand from the database companies that produce written information and auxiliary labels that the systems are programmed to automatically print out the auxiliary labels that contain the most important information for the patient regarding the safe and effective use of their medication. If the database and pharmacy systems have to be reprogrammed – which involves costs that are totally understated by this rule – then pharmacies may be unable to print out all the auxiliary labels necessary in order to accommodate the FDA required side effects statement. This could mean that the pharmacist will have to manually place the side effects statement label on the package, or the other auxiliary label that wasn't able to be printed by the computer. This will cause a disruption in efficiency pharmacy workflow, and could slow down the prescription filling process.

FDA needs to better understand how current pharmacy systems operate – and the workflow procedures in pharmacy – before the agency can make an assessment of the impact of this rule on pharmacy. Pharmacies are highly automated. The FDA's assumption that pharmacists are manually placing "stickers" on prescription vials shows a misunderstanding of the current workflow in pharmacy and understates the FDA's analysis of the total cost of this approach to pharmacies.

## **Summary and Conclusion**

In summary, NACDS believes the agency should substantially modify this proposed rule by: 1) allowing pharmacists to use discretion regarding the patients and prescriptions for which this statement is required to be distributed; 2) limiting the rule to new prescriptions only, and only for those drugs that have been marketed for less than 5 years; 3) requiring that manufacturers of prescription drugs include this statement on the PPIs, professional labeling, and unit of use prescription packages; and, 4) requiring compliance no less than one year from the rule's effective date.

The agency should take further steps to target this program to enhance its effectiveness and usefulness. As currently proposed, the agency has created a significantly burdensome program for pharmacies, and has failed to use its discretion to share the burden of implementing this program on other segments of the prescription distribution system. We appreciate your consideration of our views.

Sincerely,



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